

propofol during implantation of cardioverter defibrillator. *Eur J Anaesthesiol* 1999;16:842–7.

coupling interval, and dispersion of ventricular repolarization. *J Cardiovasc Electrophysiol* 1996;7:231–42.

## REPLY

The letter by Dr. Erdogan made some good points that, although in our view do not detract from the results and conclusions of our study, are of general interest to the issue of defibrillation success. We appreciate the opportunity to clarify the purpose of our study, which may have eluded some other readers as well.

Most patients in our study were free from antiarrhythmic drugs for five half-lives, except for two patients who had received prior amiodarone therapy that failed to suppress the targeted arrhythmia. Though we do not necessarily subscribe to the value of the 12-lead electrocardiogram as a means to demonstrate the dispersion of repolarization at the myocardial level (1,2), it is quite possible, as Dr. Erdogan states in his letter, that residual amiodarone and other factors such as anesthesia, electrolytes, autonomic tone, etc., may have influenced the dispersion of repolarization in our patients. Any of these influences might enter into the equation that governs the probabilistic nature of the defibrillation threshold (DFT), and that of the fibrillation threshold as well. However, it was not the purpose of our study to discern the effects of such factors on the DFT or ventricular fibrillation (VF) inducibility by ICD shocks.

Instead, our purpose was to show that, in a single patient and at a given time, the probability of inducibility of VF by a T-wave shock and the failure to terminate VF by a second shock were strongly associated with the extent of myocardial repolarization dispersion immediately following the shock (either caused by the shock in case of VF induction, or due to lack of synchronization by the shock in case of VF termination failure). Our intent was directed purely at the mechanistic aspects of VF induction and termination, and to demonstrate and extend for the *human* heart data derived from our earlier experimental studies (3,4), namely, that induction of functional reentry (i.e., VF) is facilitated by dispersion of repolarization with its attendant dispersion of refractoriness. Preshock dispersion is an important ingredient for post-shock dispersion to manifest itself (2), but it was beyond the scope of our study to analyze the multitude of factors that might have influenced the former.

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## REFERENCES

1. Franz MR, Zabel M. Electrophysiological basis of QT dispersion measurements. *Prog Cardiovasc Dis* 2000;42:311–24.
2. Zabel M, Klingenhoben T, Franz MR, Hohnloser SH. Assessment of QT dispersion for prediction of mortality or arrhythmic events after myocardial infarction: results of a prospective, long-term follow-up study. *Circulation* 1998;97:2543–50.
3. Behrens S, Li C, Fabritz CL, Kirchhof PF, Franz MR. Shock-induced dispersion of ventricular repolarization: implications for the induction of ventricular fibrillation and the upper limit of vulnerability. *J Cardiovasc Electrophysiol* 1997;8:998–1008.
4. Fabritz CL, Kirchhof PF, Behrens S, Zabel M, Franz MR. Myocardial vulnerability to T-wave shocks: relation to shock strength, shock

## C-Type Natriuretic Peptide and Vascular Remodeling

Morishige et al. (1) have reported local adenovirus-mediated transfer of C-type natriuretic peptide (CNP) to porcine coronary arteries, resulting in reduced stenosis of balloon-injured segments. This is an exciting development with obvious therapeutic potential. The investigators suggest several mechanisms by which CNP might regulate vascular remodeling, but they fail to mention the effects of CNP on the vascular renin-angiotensin system. Many studies have demonstrated that the natriuretic peptides have a tonic effect at various sites in the renin-angiotensin-aldosterone cascade (2), and we have demonstrated that CNP inhibits local conversion of angiotensin I to angiotensin II in the human forearm vasculature (3). These vascular effects of CNP in man in vivo are particularly relevant to the therapeutic potential of the technique described by Morishige, because of the known interspecies variability in the effects of the natriuretic peptides (2). The effects of angiotensin II on vascular remodeling are well-documented, and a reduction in local angiotensin II production is a potentially important mechanism for some of the observed effects of CNP.

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## REFERENCES

1. Morishige K, Shimokawa H, Yamawaki T, et al. Local adenovirus-mediated transfer of C-type natriuretic peptide suppresses vascular remodeling in porcine coronary arteries in vivo. *J Am Coll Cardiol* 2000;34:1040–7.
2. Wilkins MR, Redondo J, Brown LA. The natriuretic peptide family. *Lancet* 1997;349:1307–10.
3. Davidson NC, Barr CS, Struthers AD. C-type natriuretic peptide: an endogenous regulator of vascular angiotensin-converting enzyme activity. *Circulation* 1996;93:1155–9.

## REPLY

We are grateful for the opportunity to respond to the valuable comments by Drs. Davidson and Struthers concerning our recent article in the *Journal* (1). In our article, we showed that adenovirus-mediated overexpression of C-type natriuretic peptide (CNP) in the porcine coronary artery suppresses vascular constrictive remodeling after balloon injury in vivo. However, as the authors pointed out, we did not mention the possible effect of CNP on the renin-angiotensin-aldosterone system, mainly because we did not specifically examine this system in our study.

It is indeed possible that CNP/cGMP cascade may suppress the vascular remodeling through various mechanisms, including smooth muscle relaxation and inhibition of proliferation and migration of smooth muscle cells and subsequent extracellular